

# Transplant rejection

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**Transplant rejection** occurs when the immune system of the recipient of a transplant attacks the transplanted organ or tissue. This is because a normal healthy human immune system can distinguish foreign tissues and attempts to destroy them, just as it attempts to destroy infective organisms such as bacteria and viruses.

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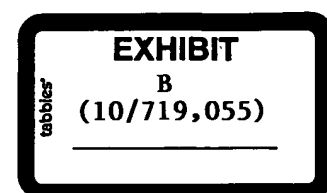
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## Types of rejection

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### Hyperacute rejection

Hyperacute rejection is a complement-mediated response in recipients with pre-existing antibodies to the donor (for example, ABO blood type antibodies). Hyperacute rejection occurs within minutes and the transplant must be immediately removed to prevent a severe systemic inflammatory response. Rapid coagulation of the blood occurs. This is a particular risk in kidney transplants, and so a prospective cytotoxic crossmatch is performed prior to kidney transplantation to ensure that antibodies to the donor are not present. For other organs, hyperacute rejection is prevented by transplanting only ABO-compatible grafts. Hyperacute rejection is the likely outcome of xenotransplanted organs.



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## Acute rejection

Acute rejection is antibody-mediated. It generally first occurs around five to ten days after a transplant if the patient is not taking immunosuppressant drugs. However, since all transplant recipients are given immunosuppressants, acute rejection can take months to develop. It can destroy the transplant if it is not recognised and treated appropriately. It occurs in around 60-75% of first kidney transplants, and 50 to 60% of liver transplants. A single episode is not a cause for concern if recognised and treated promptly, but recurrent episodes are associated with chronic rejection and graft failure. The immune system is responding to the mismatch of Major Histocompatibility Complex (MHC) proteins. MHC proteins uniquely identify tissues because they are highly variable between individuals. Identical twins and cloned tissue do match on MHC. This type of rejection is the primary reason why transplant patients have to take immunosuppressant drugs for the rest of their lives.

The above is only one type of acute rejection - acute humoral rejection. Just as important is acute rejection due to cell-mediated destruction by cytotoxic T cells.

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## Chronic rejection

Chronic rejection was a term used to describe all long term loss of function in organ transplants associated with fibrosis of the internal blood vessels of the transplant, but this is now termed chronic allograft vasculopathy and the term *chronic rejection* is reserved for those cases where the process is shown to be due to a chronic alloreactive immune response. It can be caused by a member of the Minor Histocompatibility Complex such as the H-Y gene of the male Y chromosome. This usually leads to need for a new organ after a decade or so.

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## Rejection Mechanisms

Rejection is an adaptive immune response and is mediated through both T cell mediated and humoral immune (antibodies) mechanisms. The number of mismatched alleles determines the speed and magnitude of the rejection response. Different grafts usually have a proclivity to a certain mechanism of rejection.

Organ/tissue	Mechanism
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Blood	Antibodies (isohaemagglutinins)
Kidney	Antibodies, CMI
Heart	Antibodies, CMI
Skin	CMI
Bonemarrow	CMI
Cornea	Usually accepted unless vascularised, CMI

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## Prevention of rejection

Rejection is prevented with a combination of drugs including:

- **Calcineurin inhibitors**
  - Ciclosporin
  - Tacrolimus
- **mTOR inhibitors**
  - Sirolimus
  - Everolimus
- **Anti-proliferatives**
  - Azathioprine
  - Mycophenolic acid
- **Corticosteroids**
  - Prednisolone
  - Hydrocortisone
- **Antibodies**
  - Monoclonal anti-IL-2R $\alpha$  receptor antibodies
    - Basiliximab
    - Daclizumab
  - Polyclonal anti-T-cell antibodies
    - Anti-thymocyte globulin (ATG)
    - Anti-lymphocyte globulin (ALG)

Generally a *triple therapy* regimen of a calcineurin inhibitor, an anti-proliferative, and a corticosteroid is used, although local protocols vary. Antibody inductions can be added to this, especially for high-risk patients and in the United States. mTOR inhibitors can be used to provide calcineurin-inhibitor or steroid-free regimes in selected patients.

A bone marrow transplant allows the chimeric body's immune system to adapt and accept a new organ. This requires that the bone marrow, which produces the immune cells, be from the same person as the organ donation (or an identical twin or a clone). Bone marrow is not attacked by the body's immune system, and is the only known type of transplant that has this quality. However, there is a risk of graft versus host disease (GVHD) in which the immune cells arising from the bone marrow transplant recognise the host tissues as foreign and attack and destroy them accordingly.

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## Treatment of rejection

Acute rejection is normally treated initially with a short course of high-dose methylprednisolone, which is usually sufficient to treat successfully. If this is not enough, the course can be repeated or ATG can be given. Acute rejection refractory to these treatments may require plasma exchanges to remove antibodies to the transplant.

The monoclonal anti-T cell antibody OKT3 was formerly used in the prevention of rejection, and is occasionally used in treatment of severe acute rejection, but has fallen out of common use due to the severe cytokine release syndrome and late post-transplant lymphoproliferative disorder, which are both commonly associated with use of OKT3; in the United Kingdom it is available on a named-patient use basis only.

Acute rejection usually begins after the first week of transplantation, and most likely occurs to some degree in all transplants (except between identical twins). It is caused by mismatched HLA antigens that are present on all cells. HLA antigens are polymorphic therefore the chance of a perfect match is extremely rare. The reason that acute rejection occurs a week after transplantation is because the T-cells involved in rejection must differentiate and the antibodies in response to the allograft must be produced before rejection is initiated. These T-cells cause the graft cells to lyse or produce cytokines that recruit other inflammatory cells, eventually causing necrosis of allograft tissue. Endothelial cells in vascularized grafts such as kidneys are some of the earliest victims of acute rejection. Damage to the endothelial lining is an early predictor of irreversible acute graft failure. The risk of acute rejection is highest in the first 3 months after transplantation, and is lowered by immunosuppressive agents in maintenance therapy. The onset of acute rejection is combatted by episodic treatment.

Chronic rejection is irreversible and cannot be treated effectively. The only definitive treatment is re-transplantation, if necessary. This would typically be ten years after a transplant, and this may entail returning to a transplant queue.

[[edit](#)]

## External links

- [The Immune Tolerance Network](#)

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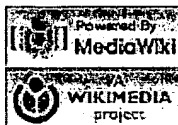
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